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Journal of Affective Disorders 97 (2007) 1–4

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Special article

Testing the Paleolithic-human-warfare hypothesis of blood–injection phobia in the Baltimore ECA Follow-up Study—Towards a more etiologically-based conceptualization for DSM-V

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Received 17 November 2005; accepted 15 June 2006
Available online 24 July 2006

Abstract

Objective: The research agenda for the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) has emphasized the need for a more etiologically-based classification system, especially for stress-induced and fear-circuitry disorders. Testable hypotheses based on threats to survival during particular segments of the human era of evolutionary adaptedness (EEA) may be useful in developing a brain-evolution-based classification for the wide spectrum of disorders ranging from disorders which are mostly overconsolidationally such as PTSD, to fear-circuitry disorders which are mostly innate such as specific phobias. The recently presented Paleolithic-human-warfare hypothesis posits that blood–injection phobia can be traced to a "survival (fitness) enhancing" trait, which evolved in some females of *reproductive-age* during the millennia of intergroup warfare in the Paleolithic EEA. The study presented here tests the key *a priori* prediction of this hypothesis—that current blood–injection phobia will have *higher* prevalence in reproductive-age women than in post-menopausal women.

Method: The Diagnostic Interview Schedule (version III-R), which included a section on blood and injection phobia, was administered to 1920 subjects in the Baltimore ECA Follow-up Study.

Results: Data on BII phobia was available on 1724 subjects (1078 women and 646 males). The prevalence of current blood–injection phobia was 3.3% in women aged 27–49 and 1.1% in women over age 50 (OR 3.05, 95% CI 1.20–7.73). [The corresponding figures for males were 0.8% and 0.7% (OR 1.19, 95% CI 0.20–7.14)].

Conclusions: This epidemiological study provides one source of support for the Paleolithic-human-warfare (Paleolithic-threat) hypothesis regarding the evolutionary (distal) etiology of bloodletting-related phobia, and may contribute to a more brain-evolution-based re-conceptualization and classification of this fear circuitry-related trait for the DSM-V. In addition, the finding reported here may also stimulate new research directions on more proximal mechanisms which can lead to the development of evidence-based psychopharmacological preventive interventions for this common and sometimes disabling fear-circuitry disorder.

Keywords: Brain evolution; Sexual selection; Mate choice; War; Anxiety disorders

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doi:10.1016/j.jad.2006.06.014

1. Introduction

The recently published research agenda for the forthcoming Diagnostic and Statistical Manual of Mental Disorders (DSM-V) has emphasized the need for a renewed focus on etiology in the DSM-V classification (Charney et al., 2002), and several authorities (Akiskal and Akiskal, 2005) have persuasively argued for an evolutionary conceptualization of the origins of psychopathology. We have argued elsewhere that testable/falsifiable predictions based on neuroevolutionary biology may be useful in developing an etiologically-based conceptualization and classification of the spectrum ranging from overconsolidational disorders (e.g., PTSD) (Bracha, 2006), to pseudo-neurological disorders (Bracha et al., 2005a,b,c), pseudo-rheumatological muscular–skeletal pain stress disorders (Bracha et al., 2005a,b,c) and pseudo-cardiological disorders such as some phobias (Bracha, 2004; Bracha et al., 2005a,b,c; Bracha, 2006).

Data from the Baltimore Epidemiologic Catchment Area (ECA) Follow-up study (Eaton et al., 1997; Bienvenu and Eaton, 1998) present a unique opportunity to examine possible evolutionary factors in the etiology of blood and injection phobia. The Baltimore ECA follow-up study was unique in that it included a specific section on blood–injection–injury type specific phobia (BIITSP). Though other epidemiological studies have included queries for blood–injection–injury fears, these have been lumped with other specific fears, so it has not been possible to differentiate types of specific phobia in subjects with multiple specific fears.

An extensive literature including several landmark twin studies suggests that the majority of reliable population variance in blood–injection fears/phobias is due to genetic, "firm-wired" factors (Kendler et al., 1999, 2001, 2002a,b). Irrational blood–injection fears are most likely polygenic or oligogenic, however, we have recently proposed that some of the alleles predisposing to blood–injection phobia in extant humans are brain-expressed allele variants of mid-Paleolithic neuroevolutionary time-depth. We have previously argued that one or more of the loci involved in blood–injection fears may carry hormonally sensitive allele variants (in a balanced/stable polymorphism). We hypothesized that the transcription of (and thus phenotypic expression of) some of these allele variants may be dependent on an individual's estrogen-to-androgen ratio.

The above hypothesis of the evolutionary (distal/ultimate) etiology of blood–injection fears (Bracha, 2004; Bracha et al., 2005a,b,c) is based on studies of male lineages through the Y-chromosome (Underhill et al., 2001), female lineages through mtDNA (Seielstad et al., 1998) and on prehistoric human remains (LeBlanc and Register, 2003). The above studies suggest that combat in the mid-Paleolithic occurred almost exclusively between mate-less young males, with reproductive-age females serving as the main object of competition. During mid-Paleolithic intergroup warfare, victors killed a high percentage of post-pubertal males (estimates range from 15% to 50%) and took reproductive-age females (and some children) captive (LeBlanc and Register, 2003). Thus, a phobic response at the sight of blood or an approaching sharp object held by a stranger was probably non-fitness enhancing in Paleolithic post-pubertal males, resulting in death or lower mate availability (or at least lower mate hierarchy). In contrast, a phobic response at the sight of blood or an approaching sharp object may have been fitness enhancing for Paleolithic reproductive-age females (and some children) since it increased the likelihood of being taken captive rather than being killed. We have therefore proposed that blood–injection fears in extant humans may be triggered by modern stressors that share stimulus properties with mid-Paleolithic intergroup human warfare, which as we note above, called for dissimilar acute fear responses in reproductive-age females versus reproductive-age males (Bracha, 2004; Bracha et al., 2005a,b,c).

There are several testable and falsifiable predictions that follow from the above Paleolithic-human-warfare hypothesis. In this study, we tested the key prediction of the Paleolithic-human-warfare hypothesis using a general population sample. Specifically, we examined whether *current* blood–injection phobia has higher prevalence in reproductive-age women than in post-menopausal women.

2. Methods

The ECA program was an epidemiologic investigation of psychopathology in adults (18 years of age and older) in five U.S. communities, conducted in the early 1980s. It employed trained lay interviewers who administered the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (Robins et al., 1981). In the Baltimore ECA Follow-up Study, conducted from 1993 to 1996, 88% of the 3481 subjects from the original Baltimore cohort were traced, and 73% of those alive ($n=1920$) were re-interviewed using the III-R version of the DIS (Robins et al., 1981) (updated to make DSM-III-R diagnoses). In the case of BIITS phobia, the diagnostic criteria are similar in DSM-III-R and DSM-IV (Bienvenu and Eaton, 1998). Written informed consent was obtained after a description of the study to the subjects. Eaton et

al. (1997) describe the methodology in more detail elsewhere.

The blood–injury section of the DIS (III-R) starts by asking if the subject has ever had such an unreasonable fear of seeing blood, getting an injection, or going to the dentist, that he or she tried to avoid it. Those who do not respond affirmatively are passed out of the section. In order to meet criteria for a DSM-IV specific phobia, the fear(s) have to be persistent (lasting months to years); almost always provoke extreme nervousness or panic; be recognized as unreasonable; and cause significant interference in social, occupational, or other routine activities (or the subject has to have marked distress about having the fear). The only DSM-IV (and DSM-III-R) criterion not addressed with this interview is that the anxiety or avoidance is not better accounted for by another mental disorder (Bienvenu and Eaton, 1998).

In this paper, we limited our focus to subjects with BIITSP who had blood and/or injection fears (not just dental fears). That is, we *a priori* excluded subjects with only dental phobia because of the likely heterogeneous etiology of this condition. Results of several studies (Davey, 1989; Moore et al., 1991; Milgrom et al., 1992, 1995; de Jongh et al., 2002) suggest that most dental phobia patients acquired their phobia by direct conditioning following a painful or extremely frightening dental experience, see Bracha et al. (in press) for a review.

3. Results

The Baltimore ECA Follow-up study included 1920 subjects who were interviewed. Some of these were cognitively impaired, and, combined with the small numbers of missing items for the BIITSP diagnosis, there were 1724 available for analysis (1078 women and 646 men). Of the women aged 50–64, only 10% still had menstrual periods; of those aged 65 or older, none did. Of women aged 40–49, only 68% still had menstrual periods; of those aged 27–39, 91% did (note: absence of menses was due to surgery in some of the women). We therefore felt confident that age would serve as an effective proxy variable for menopausal status. Results are presented as odds ratios in the table below. The prevalence of current blood–injection phobia was 3.3% in women aged 27–49 and 1.1% in women over age 50 (OR 3.05, 95% CI 1.20–7.73). The corresponding figures for males were 0.8% and 0.7% (OR 1.19, 95% CI 0.20–7.14; Table 1).

Table 1
Current blood–injection phobia by sex and age group

	Current blood–injection phobia		Prevalence	Odds ratio	95% CI
	Present	Absent			
Females					
27–49	18	523	3.3%	3.05	1.20–7.73
≥50	6	531	1.1%	1.00	Reference
Males					
27–49	3	358	0.8%	1.19	0.20–7.14
≥50	2	283	0.7%	1.00	Reference

CI=confidence interval.

4. Discussion

This study is the first to demonstrate that, as predicted by the Paleolithic-human-warfare hypothesis of blood–injection phobia (Bracha, 2004; Bracha et al., 2005a,b,c) adult women of reproductive age (operationally defined as younger than age 50) have a significantly *higher* prevalence of blood–injection phobia compared to adult women likely to be menopausal. This finding, particularly if replicated, may have taxonomic implications and contribute to a more brain-evolution-based re-conceptualization and re-categorization of fear circuitry-related disorders in the DSM-V and to a better classification of the wide spectrum of syndromes ranging from conditioned fear-memory trace overconsolidation disorders to innate fear-circuitry disorders.

Previous studies focusing on blood–injection phobia are difficult to compare with this study or with each other, since the definitions of blood–injection phobia differ greatly from one study to another. We think it useful to consider blood–injection phobia separately from dental-only phobia, which in many cases could have a different mode of acquisition (Davey, 1989; Moore et al., 1991; Milgrom et al., 1992, 1995; de Jongh et al., 2002).

The goal of this study was to contribute to a more evolutionary conceptualization of blood–injection phobia in the DSM-V. However, the finding reported here may also stimulate new clinical research directions on more proximal mechanisms which can lead to the development of science-based preventive interventions for this common and sometimes disabling fear-circuitry disorder. For example, it may be warranted to study whether brief pre-treatment with pleiotropic androgens such as dehydroxyepiandrosterone sulfate (DHEA-S) increases stress resilience in predisposed individuals during exposure to stimuli which trigger clinically significant blood–injection fears.

Acknowledgements

This material is based upon work supported in part by the Office of Research and Development, Medical

Research Service, Department of Veterans Affairs, VA Pacific Islands Health Care System, Spark M. Matsunaga Medical Center. Support was also provided by a National Alliance for Research on Schizophrenia and Depression (NARSAD) Independent Investigator Award, and the VA National Center for Posttraumatic Stress Disorders and by NIMH Grant MH 47447. The authors thank Stacy Lenze, Michelle Tsang, and Jessica Shelton for their outstanding editorial assistance.

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